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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,905	08/16/2001	Christopher Thomas Privalle	35780/238028 (5780-4)	1628

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	4

DATE MAILED: 03/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,905	PRIVALLE ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: At page 1, line 2, "is a continuation" should be changed to "claims the benefit" so that the standard terminology for a priority claim under 35 U.S.C. 119(e) is used. See MPEP 201.11 under "Reference To First Application." Correction is required.

2. Claims 1-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite because the preamble indicates that a chemically modified hemoglobin "solution" is to be prepared, whereas the last step of the claim indicates that a "composition" comprising a chemically modified hemoglobin is isolated. It is not clear if the solution of the preamble and the composition of step (c) are the same, or if step (c) implies the need for a further step of converting the composition into the solution. Claim 21 is indefinite for analogous reasons. At claim 1, line 9, "antioxidant enzyme" should be changed to "endogenous antioxidant enzymes" so that the claim terminology is consistent with that at line 5 of the claim and so that it is clear that the enzymes being referred to are the same. At claim 1, lines 9-10, the phrase "at least one endogenous antioxidant polypeptide" is unclear because there is no previous mention of endogenous antioxidant polypeptides in the claim, and it is not clear how this substance corresponds to the previously recites enzymes. There is no antecedent basis in the claims for the phrase "the endogenous antioxidant enzymes" at claim 2, lines 1-2. Note that claim 1 instead recites "antioxidant enzyme" and "endogenous antioxidant polypeptide". The purpose of the use of the company name "AG Technology" in claim 4 is not clear. It is not clear if the claim is specifying the source of the filter to be used, or if some sort of functional

definition of the filter is intended. In general, the use of trademarks in claims renders the claims indefinite. See MPEP 2173.05(u). For similar reasons, claim 12 is also indefinite. At claim 11, the phrase "at least one second filtration means" is unclear because, assuming serial placement of filtration means, there can be only be exactly one second filtration means. There is no antecedent basis in the claims for the phrase "said isolated modified hemoglobin solution" in claim 19. There is no antecedent basis in the claim for the phrase "said endogenous antioxidants" at claim 22, line 3. Note that line 2 of the claim uses the terminology "endogenous antioxidant enzyme". At claim 35, line 3, "solution" should be inserted after "hemoglobin" so that there is direct antecedent basis in the claims for the claim terminology.

3. Claims 31-34 are objected to because of the following informalities: At claim 31, line 2, "superoxide" is misspelled. At claim 32, line 2, the word "a" (third occurrence) should be deleted. Appropriate correction is required.

4. Instant claims 1-35 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/253,758 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the instant claimed invention.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

6. Claims 22-35 are rejected under 35 U.S.C. 102(a) as being anticipated by the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 507-1517). The Privalle et al article teaches pyridoxylated hemoglobin polyoxyethylene conjugate (PHP) which additionally comprises soluble red blood cell enzymes, including catalase and superoxide dismutase. The PHP is used in Phase II and Phase III clinical trials as a nitric oxide scavenger, e.g. in the treatment of septic shock. In general, hemoglobin-based therapeutics are described as being useful for blood replacement during surgery. See, e.g., the Abstract; page 1507; page 1514, paragraph bridging columns 1 and 2; and page 1515, column 1, last paragraph. Because the PHP

compositions of the Privalle et al article are described as being used in Phase II and Phase III clinical trials, they are deemed inherently to be free of viral contamination to the same extent claimed by Applicants because the use of virally contaminated products is not permitted. Sufficient evidence of similarity is deemed to be present between the PHP of the Privalle et al article and the hemoglobin solution recited in Applicants' claims to shift the burden to Applicants to provide evidence that the hemoglobin solution recited in Applicants' claims is unobviously different than the PHP of the Privalle et al article. Note that even though the Privalle et al article does not teach or suggest a filtering method for producing its PHP, a novel and unobvious process of making a product does not necessarily result in a novel and unobvious product.

7. Claims 22-35 are rejected under 35 U.S.C. 103(a) as being obvious over the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 507-1517). Application of the Privalle et al article is the same as in the above rejection of claims 22-35. To the extent that the Privalle et al article does not teach a hemoglobin solution of the same degree of purity as is recited in Applicants' claims, it would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to subject the PHP of the Privalle et al article to any known or combination of known purification procedures in order to reduce the viral contamination of the PHP, because it is known that blood products are susceptible to viral contamination, because it is desirable in the art to minimize viral contamination of all medical products in order to improve their safety, and because the use of known purification procedures in order to achieve only the expected purification is prima facie obvious.

8. Claims 22-35 are rejected under 35 U.S.C. 102(b) as being anticipated by the Privalle et

al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254). The Privalle et al abstract teaches pyridoxylated hemoglobin polyoxyethylene conjugate (PHP) which additionally comprises soluble red blood cell enzymes, including catalase and superoxide dismutase. The PHP is used in clinical trials as a nitric oxide scavenger, e.g. in the treatment of NO-induced shock characterized by hypotension. In general, hemoglobin-based therapeutics are described as being useful for blood replacement during surgery. Because the PHP compositions of the Privalle et al abstract are described as being used in clinical trials, they are deemed inherently to be free of viral contamination to the same extent claimed by Applicants because the use of virally contaminated products is not permitted. Sufficient evidence of similarity is deemed to be present between the PHP of the Privalle et al abstract and the hemoglobin solution recited in Applicants' claims to shift the burden to Applicants to provide evidence that the hemoglobin solution recited in Applicants' claims is unobviously different than the PHP of the Privalle et al abstract. Note that even though the Privalle et al abstract does not teach or suggest a filtering method for producing its PHP, a novel and unobvious process of making a product does not necessarily result in a novel and unobvious product.

9. Claims 22-35 are rejected under 35 U.S.C. 103(a) as being obvious over the Privalle et al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254). Application of the Privalle et al abstract is the same as in the above rejection of claims 22-35. To the extent that the Privalle et al abstract does not teach a hemoglobin solution of the same degree of purity as is recited in Applicants' claims, it would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to subject the PHP of the Privalle et al abstract to any known or combination of known purification procedures in order to reduce the

viral contamination of the PHP, because it is known that blood products are susceptible to viral contamination, because it is desirable in the art to minimize viral contamination of all medical products in order to improve their safety, and because the use of known purification procedures in order to achieve only the expected purification is prima facie obvious.

10. Claims 1-21 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. The prior art of record does not teach or fairly suggest filtering a mixture of hemoglobin and endogenous antioxidant enzymes in order to render the mixture substantially free of viral contamination. Note that the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 507-1517) and the Talarico et al article (Biochim. Biophys. Acta, Vol. 1476, pages 53-65) do not teach or suggest filtration as a viral purification method; that D'Agnillo et al (U.S. Patent No. 5,606,025; see column 3, lines 11-15) teach purification steps could result in the separation of enzymes from hemoglobin; and that Tye (U.S. Patent No. 4,529,719) teaches the desirability of removing all non-heme proteins, which would include antioxidant enzymes, from stroma-free hemoglobin solutions.

Winslow is cited as art of interest, showing that it is known to add antioxidants and enzymes such as peroxidases, catalase, and superoxide dismutase to hemoglobin solutions (see column 34, lines 34-44).

11. With respect to the Information Disclosure Statement filed February 7, 2002, Reference 30 is crossed off because no copy of this reference was provided. (Instead, two copies of Reference 29 were provided.) Reference 39 is crossed off because no copy of this reference was

provided. .If Applicants will submit a copy of these two references with their next response, the examiner will consider them and make them of record.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

March 4, 2003